

D¹ cont.
as plasma-derived protein C, and wherein said transgenic mammal is selected from the group consisting of mice, rats, rabbits, pigs, sheep, goats and cows.

10/8/81
heterologous
5. (Twice amended) A process for the production of protein C, comprising the steps of:

Mr 12/17
(A) providing a non-human transgenic mammal characterized by an exogenous DNA sequence stably integrated in its genome, wherein said exogenous DNA sequence comprises the 5' 4.2 kb *Sau*3A - *Kpn*1 promoter of the mouse whey acidic protein gene, operably linked to a DNA sequence encoding protein C and a signal peptide, said promoter being specifically active in mammary cells and said signal peptide being effective in directing the secretion of said protein C into the milk of said transgenic mammal, and wherein said transgenic mammal is selected from the group consisting of mice, rats, rabbits, pigs, sheep, goats and cows;

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(B) producing milk from said transgenic mammal, wherein said milk contains said secreted protein C, and wherein the activated form of said secreted protein C has an enzymatic activity of at least 50% as plasma-derived protein C;

(C) collecting said milk; and

(D) isolating said protein C from said milk.

Sub. 10/8/81
D³
11. (Thrice amended) A process for producing non-human transgenic [animals] mammals, comprising the steps of (A) providing a mixture containing a double-stranded DNA; (B) subjecting said mixture to anion-exchange high performance liquid chromatography to obtain purified double-stranded DNA; and thereafter (C) microinjecting an aqueous buffer solution containing said purified double-stranded DNA into an animal embryo, wherein said double-stranded DNA is selected from the group consisting of a double-stranded DNA comprising the 5' 4.2 kb *Sau*3A - *Kpn*1 promoter fragment of the mouse whey acidic protein promoter, a double-stranded DNA comprising a fragment of

Sub E2
the human protein C gene beginning 21 basepairs upstream of the protein C start codon and ending at the *NheI* site in the 3' end of the protein C gene, and a double-stranded DNA comprising a DNA sequence consisting essentially of the 5' 4.2 kb *Sau3A* - *Kpn1* promoter fragment of the mouse whey acidic protein promoter ligated directly or by a linker to a fragment of the human protein C gene beginning 21 basepairs upstream of the protein C start codon and ending at the *NheI* site in the 3' end of the protein C gene, wherein the activated form of protein C encoded by said double-stranded DNA has an enzymatic activity of at least 50% as plasma-derived protein C, and wherein said transgenic mammal is selected from the group consisting of mice, rats, rabbits, pigs, sheep, goats and cows.

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JL heterologous (Twice amended) A process for the production of a polypeptide in the milk of a transgenic non-human mammal, comprising the steps of:

Ex 42
D3 cont
(A) providing a non-human transgenic mammal characterized by an exogenous DNA sequence stably integrated in its genome, wherein said exogenous DNA sequence comprises the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene, operably linked to a DNA sequence encoding said polypeptide and a signal peptide, said promoter being specifically active in mammary cells and said signal peptide being effective in directing the secretion of said polypeptide into the milk of said transgenic mammal[, and wherein said transgenic mammal is selected from the group consisting of mice, rats, rabbits, pigs, sheep, goats and cows];

- JL
- (B) producing milk from said transgenic mammal, wherein said milk contains said secreted polypeptide;
 - (C) collecting said milk; and
 - (D) isolating said polypeptide from said milk.

D4
14. (Twice amended) A transgenic non-human mammal containing an exogenous DNA sequence stably integrated in its